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Document Control Office
Office of Pesticides and Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

94 JUN 29 AM 7:57

RECEIVED

Re: TSCA Section 8(e) Notification for Di-tert-butyl Dicarbonate

Dear Sir or Madam:

First Chemical Corporation is submitting this notice as may be required by Section 8(e) of the Toxic Substances Control Act (TSCA) and EPA's Statement of Interpretation and Enforcement Policy, 43 Fed. Reg. 1110 (March 16, 1978).

The basis for this submission is the results of a dermal sensitization study (closed patch repeated insult) in guinea pigs with di-tert-butyl dicarbonate (DBDC), CAS No. 24424-99-5. The study was carried out by Ricerca, Inc., Painesville, OH. A 4.5% concentration of DBDC produced moderate or severe erythema in all test animals at challenge. Edema was also noted at 24 hours. At 48 hours, additional findings were edema, blanching, necrosis and eschar.

DBDC is manufactured in the US for use as an intermediate in the synthesis of peptides. It was the subject of an earlier 8(e) notification based on its acute toxicity by the inhalation route (submission dated 9-29-92).

We do not believe the results of this study reasonably support a conclusion that DBDC presents a substantial risk of injury to health for the following reasons:

1. DBDC is handled in an enclosed system by First Chemical Corporation and by its customers, which are pharmaceutical companies.

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Document Control Office
Office of Pesticides and Toxic Substances
U.S. Environmental Protection Agency
June 23, 1994

2. Dermal exposure is controlled by the use of polycoated TYVEK suits and neoprene gloves.

3. The high acute toxicity by inhalation is noted on our MSDS and further warns workers to avoid exposure to DBDC.

4. We are not aware of any instances of sensitization in humans from exposure to DBDC.

Nevertheless, we are submitting a copy of the report at this time because it may meet the Agency's criteria for submission based on production increases.

A copy of the current Material Safety Data Sheet and the report are enclosed.

Please contact the undersigned if you need additional information pertaining to this submission.

Sincerely yours,

FIRST CHEMICAL CORPORATION

Steven C. Dawson

Steven C. Dawson, CIH
Manager, Industrial Hygiene
and Health

SCD

Enclosures

Quality Chemicals, Inc.
Subsidiary of First Chemical Corporation

P.O. Box 216
Industrial Park
Tyrone, Pennsylvania 16686

Telephone (814) 684-4310
Fax (814) 684-2532

MATERIAL SAFETY DATA SHEET

PRODUCT NAME: DI-T-BUTYL DICARBONATE

SECTION 1 - IDENTITY

Product Name:	DI-T-BUTYL DICARBONATE
Synonyms:	DBDC: Bis(1,1-dimethylethyl) dicarbonate
CAS Number:	24424-99-5
Chemical Family:	Dicarbonate
Formula:	$C_{10}H_{18}O_5$

SECTION 2 - HAZARDOUS INGREDIENTS

COMPONENT	%	OSHA-PEL	ACGIH-TLV
Di-t-butyl Dicarbonate	95.0 MIN.	None	None

SECTION 3 - PHYSICAL DATA

Boiling Point:	133-135°F (56-57°C) @ 0.5mm
Specific Gravity:	0.95
Vapor Density (Air = 1):	Not Available
Evaporation Rate:	Not Available
Appearance and Odor:	Clear liquid or solid depending on temperature.
Melting Point:	73.4°F (23°C)
Solubility in Water:	Insoluble
Vapor Pressure (mmHg):	Not Available

SECTION 4 - FIRE AND EXPLOSION HAZARD DATA

Flash Point: >200°F (>93°C) **Method:** Tag Closed Cup (TCC)

Auto-ignition Temperature: Not available

Flammable Limits in Air, % by Volume: Lower: Not Available
Upper: Not Available

Extinguishing Media:

Water, carbon dioxide, dry chemical.

Special Fire Fighting Procedures:

Wear full protective clothing with self-contained positive pressure breathing apparatus. If there is potential for skin exposure to Di-t-butyl dicarbonate, see Section 8 of this MSDS. Use water spray to cool containers.

Unusual Fire and Explosion Hazards:

This material will burn with the release of potentially toxic gases. The release of carbon dioxide upon heating can result in container rupture or container explosion.

SECTION 5 - REACTIVITY DATA

Stability:

Stable at normal temperatures and conditions of storage. Unstable in conditions of high heat.

Incompatibility:

Strong acids, bases, oxidizing and reducing agents.

Hazardous Decomposition Products:

Carbon dioxide.

Hazardous Polymerization:

Will not normally occur.

SECTION 6 - HEALTH HAZARD DATA

Primary Route(s) of Entry:

Inhalation, ingestion, skin absorption.

Effects of Overexposure:

Inhalation:

Inhalation of this material may cause severe lung damage. Repeated inhalation of low concentrations of this material may aggravate pre-existing chronic lung diseases.

Ingestion:

Ingestion may irritate the gastrointestinal tract.

Skin Contact:

Contact with this material may cause moderate skin irritation. There was evidence of dermal sensitization when guinea pigs were exposed to this material.

Eye Contact:

This material is considered to be a moderate eye irritant.

Other Effects:

No further health effects are known.

Other Toxicity Data:

Inhalation:	LC_{50}	-	Rats (0.10mg/L/4hr)
Ingestion:	LD_{50}	-	Rats (>5,000 mg/kg)
Skin Contact:	LD_{50}	-	Rabbits (>2,000 mg/kg) (Primary Dermal Irritation Index - rabbits - 3.5-moderate irritant)

Eye Contact:

Rabbit - Mean total score of 12 according to the Draize method for grading ocular effects (moderate irritant). Conjunctival irritation was observed at 1 hour and persisted on some animals through day 4 of the study (moderate eye irritant).

Medical Conditions Aggravated by Exposure:

Pre-existing chronic lung diseases.

Carcinogenicity:

Contains No CBI

National Toxicology Program (NTP): Not listed

IARC Monographs: Not Listed

OSHA: Not Listed

ACGIH: Not Listed

Emergency and First Aid Procedures:

Inhalation:

Remove to fresh air immediately. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Consult a physician.

Ingestion:

Immediately induce vomiting as directed by a physician. Repeat until vomit is clear. Never give anything by mouth to an unconscious person. Consult a physician.

Skin Contact:

Immediately flush skin with water for at least 15 minutes while removing contaminated clothing and shoes. If redness or irritation occurs, seek medical attention. If breathing is difficult, give oxygen. Never give alcohol in any form.

Eye Contact:

Flush with water for at least 15 minutes. Have eyes examined and treated by a physician.

NOTE TO PHYSICIAN:

No additional information is available.

SECTION 7 - SPILL OR LEAK PROCEDURES

Steps to be Taken in Case Material is Released:

Evacuate area and keep personnel upwind. Cut off any source of ignition and ventilate spill area. Contain spill with absorbent material. Transfer absorbent and other contaminated materials to a DOT approved covered metal container for disposal. Consult with Federal, State, and local regulatory agencies to determine acceptable clean-up levels. Comply with Federal, State, and local regulations on reporting releases.

Disposal Method:

Consult 40 CFR Parts 261 and 268, State, and local regulations for guidance on disposal of this product. Incineration at a facility with proper Federal and State issued permits is the recommended method for disposal.

Section 313 Supplier Notification:

This material is not subject to the reporting requirements of Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 and of 40 CFR 372.

EPA Waste Identification Number: None.

Reportable Quantity (RQ):

This material is not regulated under 40 CFR 117.3. Comply with Federal, State, and local regulations on reporting releases.

Container Disposal:

Empty containers may retain product residue. Observe all hazard precautions. Keep away from heat, sparks, and flames. Do not distribute, make available, or reuse empty container except for storage and shipment of original product. Remove all product residue, and puncture or otherwise destroy empty container before disposal. Consult Federal, State and local regulations for guidance on disposal.

SECTION 8 - SPECIAL PROTECTION INFORMATION

Respiratory Protection:

If vapors are present, use, as a minimum, a NIOSH approved full face respirator with canisters or cartridges specifically approved for use with organic vapors. Whenever cartridges or canister respirators are used, insure the frequent changing of the filter element. Use a supplied air respirator when in doubt of the atmospheric concentration. Consult 29 CFR 1910.134 regarding use of respirators.

Protective Clothing:

Take all precautions to prevent skin contact. Use neoprene gloves and polycoated TYVEK clothing. Additional protection, such as a chemical resistant full body suit may be required depending upon conditions.

Eye Protection:

Use chemical goggles and a full face shield if splashing is possible.

SECTION 9 - SPECIAL PRECAUTIONS

Storage and Handling:

Store in cool, well-ventilated areas in tightly closed containers away from acids, oxidizing agents, and other incompatible chemicals. Prevent skin and eye contact. Avoid breathing vapors. Thorough showering at the end of the work shift is strongly recommended. Work clothes should be laundered daily.

Other Comments:

Because the long term health effects from exposure to Di-T-butyl dicarbonate have not been fully evaluated, exposure should be kept to the lowest level possible. Use only under the supervision of a technically qualified individual.

Sources of Additional Information:

Established reference texts, on-line computer information services, and recent journal publications may provide additional information on the characteristics and hazards of Di-T-butyl dicarbonate.

EFFECTIVE DATE: June 23, 1994

REPLACES: June 30, 1992

PREPARED BY: Steven C. Dawson, C.I.H.
Manager, Industrial Hygiene and Health

Copy 2

RICERCA, INC.

DEPARTMENT OF TOXICOLOGY AND ANIMAL METABOLISM

STUDY TITLE

DERMAL SENSITIZATION STUDY (CLOSED-PATCH REPEATED INSULT) IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

RICERCA - DOCUMENT NUMBER:
3620-90-0239-TX-001

AUTHORS

Steven K. Shults, B.A.
Ann W. Brock, M.S.
James C. Killeen, Jr., Ph.D.

DATE STUDY COMPLETED: July 31, 1990

STUDY SPONSOR

First Chemical Corporation
1001 Industrial Highway
P. O. Box 1427
Pascagoula, Mississippi 39568

TESTING FACILITY

Ricerca, Inc.
Department of Toxicology
and Animal Metabolism
7528 Auburn Road
P. O. Box 1000
Painesville, Ohio 44077
Phone: (216) 357-3300

TESTING FACILITY - PROJECT IDENTIFICATION

Project: 90-0239

REPORT

RICERCA - DOCUMENT NUMBER: 3620-90-0239-TX-001

DISTRIBUTION

Original

Ricerca, Inc. Archives/B. J. Szollosi

Copies

Sponsor/First Chemical Corporation/S. C. Dawson (1) unbound, (2) bound

COMPLIANCE STATEMENT

RICERCA, INC.
Department of Toxicology and Animal Metabolism

The study reported herein, "Dermal Sensitization Study (Closed-Patch Repeated Insult) in Guinea Pigs with Di-tert-Butyl Dicarbonate," Ricerca Document Number 3620-90-0239-TX-001, was conducted and reported in compliance with the Good Laboratory Practice Regulations set forth in Title 40, Part 792 of the Code of Federal Regulations of the United States of America.

Steven K. Shults

Steven K. Shults, B.A.
Study Director
Ricerca, Inc.

July 31, 1990
Date

REPORT

DERMAL SENSITIZATION STUDY (CLOSED-PATCH REPEATED INSULT) IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

RICERCA - DOCUMENT NUMBER: 3620-90-0239-TX-001

Ricerca, Inc.
Department of Toxicology and Animal Metabolism
7528 Auburn Road
P. O. Box 1000
Painesville, Ohio 44077

Steven K. Shults, B.A., Research Toxicologist
Toxicology and Animal Metabolism
Study Director — July 31, 1990 Date

Ann W. Brock, M.S., Report Writer/Laboratory Assistant
Toxicology and Animal Metabolism — July 25, 1990 Date

James C. Killeen, Jr., Ph.D., Director
Toxicology and Animal Metabolism — July 25, 1990 Date

Robert A. Baxter, Vice President — July 26, 1990 Date

RICERCA, INC.

QUALITY ASSURANCE STATEMENT

Based on review of "Dermal Sensitization Study (Closed-Patch Repeated Insult) in Guinea Pigs with Di-tert-Butyl Dicarbonate," Ricerca Document Number 3620-90-0239-TX-001, it is concluded that this report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

Listed below are the dates inspections were conducted by Quality Assurance and the dates findings were reported to the Study Director and to Management.

Date(s) of Inspection	Reported to Study Director	Reported to Management
May 31, 1990	June 1, 1990	June 1, 1990
July 13, 16-18, 1990	July 18, 1990	July 18, 1990

Gilbert Claudio
Quality Assurance Supervisor

July 26, 1990
Date

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

SUMMARY

This study was conducted according to the modified Buehler method to determine the potential for the test material, Di-tert-Butyl Dicarbonate, to produce dermal sensitization in the guinea pig. Dinitrochlorobenzene (DNCB), was tested concurrently as a positive control material. During the induction phase of the study, materials were administered dermally to sites on the backs of Hartley guinea pigs once a week for three consecutive weeks. Two weeks following the last induction dose, the animals were challenged. An irritation control group was used for the materials during the challenge phase to differentiate dermal reactions produced by irritation from those produced by sensitization.

During the induction phase of the sensitization study, the test material was administered once weekly over a three week period at a 15% (v/v) concentration in 80% ethanol to one group of guinea pigs. The positive control material was administered to a second group of guinea pigs at a 0.2% (w/v) concentration in 80% ethanol during the induction phase.

During the challenge phase, the animals in the test material group received single administrations of Di-tert-Butyl Dicarbonate at approximately the maximum nonirritating concentration of 4.5% (v/v) in acetone. The animals in the positive control group received single administrations of DNCB at a 0.06% (w/v) concentration in acetone. A third group of animals (irritation controls) received, at the time of challenge only, single administrations of the same concentrations of test and positive control materials administered to the other two groups.

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

SUMMARY (Continued)

The positive control material, DNCB, did elicit dermal sensitization in the positive control group animals. This positive response demonstrated the susceptibility of the guinea pigs used in this study to dermal sensitization.

At challenge, Di-tert-Butyl Dicarbonate produced dermal responses in the test group animals which clearly were greater than the responses observed in the irritation control group animals. Therefore, it was concluded that the test material, Di-tert-Butyl Dicarbonate, demonstrated potential to produce dermal sensitization when administered by the method of Buehler to Hartley guinea pigs.

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

I. TITLE

Dermal Sensitization Study (Closed-Patch Repeated Insult) in Guinea Pigs with Di-tert-Butyl Dicarbonate.

II. INTRODUCTION AND OBJECTIVE

This study was performed according to the protocol for a dermal sensitization study in guinea pigs, Ricerca document number 3620-90-0239-TX-000. The objective of the study was to evaluate, according to the modified Buehler method, the potential for sensitization in the guinea pig with repeated dermal exposure to the test material.

III. TESTING FACILITY

Ricerca, Inc.
Department of Toxicology and Animal Metabolism
7528 Auburn Road
P. O. Box 1000
Painesville, Ohio 44077

Study Director: Steven K. Shults, B.A.

Senior Toxicology Technician: Dawn L. Freeman, A.H.T.

Report Preparation: Steven K. Shults, B.A.
Ann W. Brock, M.S.

IV. SPONSOR

First Chemical Corporation
1001 Industrial Highway
P. O. Box 1427
Pascagoula, Mississippi 39568

V. STUDY DATES

Protocol signed by Study Director: May 8, 1990

Range-Finding Study Number 1

Initiation of the Study: May 23, 1990
Termination of the Study: May 25, 1990

Range-Finding Study Number 2

Initiation of the Study: May 29, 1990
Termination of the Study: May 31, 1990

Range-Finding Study Number 3

Initiation of the Study: June 13, 1990
Termination of the Study: June 15, 1990

Range-Finding Study Number 4

Initiation of the Study: June 19, 1990
Termination of the Study: June 21, 1990

Dermal Sensitization Study

Initiation of the Induction Phase of the Study: May 31, 1990
Initiation of the Challenge Phase of the Study: June 27, 1990
Termination of In-Life Phase of the Study: June 29, 1990

VI. SUPPORTIVE DATA, PROTOCOL AND REPORT

The raw data, original protocol and original laboratory report will be maintained in the Archives of Ricerca, Inc., 7528 Auburn Road, Painesville, Ohio.

VII. MATERIALS AND METHODS

A. Test Material - Identification and Receipt

Name and/or Code Identification: Di-tert-Butyl Dicarbonate
Physical Description: clear liquid

Label Description: Di-tert Butyl Dicarbonate

The test material was received from First Chemical Corporation, on April 18, 1990. The material was stored in a secured area, at room temperature in the dark. After completion of the study, the remainder of the material will be returned to the Source.

All responsibility for specific information regarding the physical, chemical and stability properties of the test material is assumed by the Sponsor.

B. Positive Control Material - Identification and Receipt

Chemical Name: 1-chloro-2,4-dinitrobenzene
Common Name: dinitrochlorobenzene (DNCB)
Physical Description: yellow solid
Product Number: C-6396
Lot Number: 44F-0565

The positive control material was received from Sigma Chemical Company, in October 1986. The material was stored in a secured area, at room temperature in the dark.

C. Vehicles

80% Ethanol (v/v): The 200 proof ethanol was supplied by U. S. Industrial Chemicals Company. This ethanol was diluted to 80% (v/v) with deionized water. The 80% (v/v) ethanol was used for preparation of solutions of the test material administered during the range-finding testing and the induction phase of the sensitization study, and also for preparations of the positive control material administered during the induction phase of the sensitization study.

Acetone: The certified A.C.S. acetone (Product Number A18-4, Lot Number 893776) was supplied by Fisher Scientific. This acetone was used for preparation of solutions of the test material administered during the range-finding testing and the challenge phase of the sensitization study, and also for preparations of the positive control material administered during the challenge phase of the sensitization study.

D. Animals - Receipt and Husbandry

The fifty-eight Hartley guinea pigs used in this testing were selected from a group of guinea pigs received on May 16, 1990 from Murphy Breeding Laboratories, Plainfield, Indiana. Upon receipt, these animals were housed individually in suspended stainless steel cages. The animals were housed for a minimum

seven-day acclimation period prior to initiation of range-finding testing and the sensitization study. During the acclimation period, the animals were observed at least once daily for mortality and moribundity.

The air flow in the animal rooms was equal to eleven or more fresh air changes per hour. During the acclimation and study periods, the temperature and relative humidity were within the range of 67° to 75° F and 40% to 70%, respectively. A twelve hour light/dark cycle was maintained during the acclimation and study periods.

The animals received Purina® Guinea Pig Chow® (Number 5025). Feed was available ad libitum during acclimation and throughout the study. Tap water (supplied by the City of Paines-ville) was available ad libitum through an automatic watering system during both the acclimation and study periods.

E. Animals - Assignment to Study

Prior to the initiation of the study, a physical examination of the animals was conducted to determine the suitability of the animals for placement on study. All animals were considered to be healthy and acceptable for use on the study. Animal selection for the sensitization study was based on a computer-generated process of randomization of animals utilizing random numbers.

For the range-finding studies, each animal was identified by an animal number using a cage card. For the dermal sensitization study, each animal was identified permanently with an ear tag, imprinted with a unique number, and by cage card.

F. Animal Preparation

The hair at and around the site of application (back and sides) was clipped closely with an Oster Small Animal Clipper on the day prior to each application during the range-finding studies and the sensitization study.

G. Material Preparation

For the purpose of this study, the test material was considered to be 100% Di-tert-Butyl Dicarbonate. Prior to dose preparation for the first, second, and third range-finding studies and the second and third induction exposures, the container of test material was warmed in a water bath at approximately 90°F for approximately 1 hour to dissolve any crystals which had formed. This procedure was not necessary prior to dose preparation for the fourth range-finding study, the first induction exposure, and the challenge phase since crystals had not reformed. No preparation of the test material was required for the 100% (undiluted) concentration utilized for range-finding. Mixtures (v/v) of the test material were prepared with either 80% ethanol or acetone for other concentrations utilized for range-finding and the induction and challenge phases of the sensitization study. Fresh mixtures were prepared on each day of dosing. Each mixture was stirred on a stir plate with spin bar prior to and during the dosing of the animals.

Separate solutions of the positive control material, DNCB, were made for each of the concentrations tested in the sensitization study. A fresh solution (w/v) was made on each day of dosing with either 80% ethanol or acetone, as required.

H. Material Administration - General

The undiluted test material and preparations of the test and positive control materials were administered in doses of 0.4 ml per site. A 25 mm Hill Top Chamber® containing a cotton pad was utilized to maintain the respective material at each site. For each application, the material was applied (utilizing a tuberculin syringe) to the site, to the extent that the material would remain within an area the size of the chamber, and then applied to the pad in the chamber. The chamber was then applied to the site. In addition to the tape supplied, each chamber was secured with 2 inch Johnson and Johnson Dermiform tape wrapped around the trunk of the animal. Following the single or multiple applications per animal, synthetic rubber dental dam was applied over the chamber(s). The trunk of the animal was then wrapped with 3 inch Elasto-plast® bandage to firmly secure the chamber(s). The animal was returned to its cage. This procedure was repeated for each animal.

Following the six-hour exposure period, the bandaging and chamber(s) were removed from each animal. Residual material was removed by rinsing and wiping each site using water and disposable paper towels.

I. Range-Finding Studies

1. Material Administration

In order to evaluate the irritation potential of the test material (Di-tert-Butyl Dicarbonate), eighteen animals were evaluated in four range-finding studies. In the first range finding study, the guinea pigs were dosed with three concentrations of the test material and the vehicle (control), at four different sites (one concentration per

site), two on either side of the midline of the back. In the second and third studies, the guinea pigs were dosed with four concentrations of the test material at four different sites (one concentration per site), two on either side of the midline of the back. In the fourth range-finding study, the guinea pigs were dosed with one concentration of the test material at one site.

In the first range-finding study (May 23, 1990) with the test material, one of the sites on each of four animals received a maximum (undiluted) concentration of the test material. Two other sites on each animal received concentrations of 50 and 25% (v/v) of the test material in 80% ethanol. The vehicle, 80% ethanol, was applied to one site on each animal and served as a control. This study was designed to provide data for the selection of a concentration to be used for the induction phase of the sensitization study.

In the second range-finding study (May 29, 1990) with the test material, the material was applied at concentrations of 10, 4.5, 2.0 and 1.0% (v/v) in 80% ethanol to the four sites on each of four animals. This study was designed to provide additional data for the selection of a concentration to be used for the induction phase of the sensitization study.

In the third range-finding study (June 13, 1990) with the test material, the material was applied at concentrations of 10, 4.5, 2.0 and 1.0% (v/v) in acetone to the four sites on each of six animals. This study was designed to provide additional data for the selection of a concentration to be used for the challenge phase of the sensitization study.

In the fourth range-finding study (June 19, 1990) with the test material, the material was applied at a concentration of 7% (v/v) in acetone to one site on each of four animals. This study was designed to provide additional data for the selection of a concentration to be used for the challenge phase of the study.

2. Dermal Evaluations

Observations for signs of dermal responses were made at approximately 24 and 48 hours after test or control material application. At each observation interval, the scores for all treated sites were recorded.

Approximately three hours prior to the 24-hour scoring, a depilatory (Neet® Cream Hair Remover, Whitehall Laboratories, Inc., New York, New York) was used to remove hair at the sites of application. The depilatory was used on all animals treated with the test material. The depilatory was applied to the backs of the animals and allowed to remain on the skin for 10 to 15 minutes. The depilatory was then thoroughly washed off with a stream of warm running water. Animals were gently dried with disposable paper towels and returned to their cages.

J. Dermal Sensitization Study

The method employed was based on that described by E. V. Buehler in "Delayed Contact Hypersensitivity in the Guinea Pig," Arch. Dermatol. 91: 171-175, (1965) and H. L. Ritz and E. V. Buehler in "Planning, Conduct and Interpretation of Guinea Pig Sensitization Patch Tests," in Current Concepts in Cutaneous Toxicity (Victor A. Drill and Paul Lazar, eds.) pp. 25-40; Academic Press, 1980.

1. Experimental Design

The experimental design of the study was as follows:

Group	Test/Control Material	Number of Animals	Concentration	
			Induction	Challenge
1	Test Material	20 (10M, 10F)	15% (v/v)	4.5% (v/v)
2	DNCB (Positive Control)	10 (5M, 5F)	0.2% (w/v)	0.06% (w/v)
3[a,b]	Test Material (Irritation Control-Challenge)	10 (5M, 5F)	none	4.5% (v/v)
	DNCB (Irritation Control-Challenge)		none	0.06% (w/v)

[a]The irritation control group was treated at the time of challenge only. The same ten animals served as irritation controls for the test material and the positive control (DNCB).

[b]The design of the study also included a fourth group of ten animals (five males and five females) which were maintained along with the other three groups and would have served as irritation controls at the time of rechallenge, if conducted. A rechallenge was not required and the fourth group was not utilized on this study.

2. Material Administration

a. Induction Phase

During the induction phase, the test material was applied to Group 1 animals at a 15% (v/v) concentration in 80% ethanol. The positive control material, DNCB, was applied to Group 2 animals at a 0.2% (w/v) concentration in 80% ethanol. No material was applied to any animals in the irritation control group during the induction phase.

Administrations to a site on the upper right side of the midline of the back, as close to the midline as possible, were repeated once a week for three consecutive weeks, for a total of three applications per animal. For the test material, the same site on each animal was used for two induction applications. For the third induction application, the administrations were made at other sites on the right side of the back, as required. The sites for each material were changed during the third induction application, as necessary, to avoid reapplication of material to skin exhibiting qualitative changes, e.g., significantly irritated or damaged skin.

b. Challenge Phase

The single challenge was conducted fourteen days after the last induction exposure. At challenge, the test material was applied to animals in Groups 1 and 3 at a concentration of 4.5% (v/v) in acetone. The positive control material was applied to animals in Groups 2 and 3 at a concentration of 0.06% (w/v) in acetone. The irritation control animals (Group 3) treated at

the time of challenge were utilized to differentiate dermal reactions produced by irritation in the test and positive control groups from those produced by sensitization.

In the test and positive control material groups (Groups 1 and 2), the materials were administered in the same manner as during the induction phase, but at a site on the opposite side of the midline of the back from the site(s) used for induction. The irritation control animals (Group 3) were subjected to the same procedure as the animals receiving the challenge exposures. At this time, applications of the two materials (test and positive control) were made on opposite sides of the midline of the back on each control animal.

3. Dermal Evaluations

a. Induction Phase

Dermal evaluations were made at approximately 24 and 48 hours after each induction exposure. A depilatory was not utilized prior to scoring during the induction phase of this study.

b. Challenge Phase

Dermal evaluations were made at approximately 24 and 48 hours after the challenge application.

Approximately three hours prior to the 24-hour scoring, a depilatory (Neet® Cream Hair Remover, Whitehall Laboratories, Inc., New York, New York) was used to remove hair at the sites of application. The depilatory was applied to the test sites on all

animals and allowed to remain on the skin for 10 to 15 minutes. The depilatory was then thoroughly washed off with a stream of warm running water. Animals were gently dried with disposable paper towels and returned to their cages.

K. Evaluations

1. Viability Observations

All guinea pigs were observed once daily during acclimation and twice daily during both the range-finding studies and the dermal sensitization study for mortality and moribundity.

2. General Health Examinations

All guinea pigs received a general health examination once weekly during the dermal sensitization study. All observations were recorded.

3. Body Weights

Body weights were recorded within 30 hours prior to the initiation of the dermal sensitization study and following the challenge phase of the study.

4. Scoring System

Dermal responses noted during the range-finding studies and the dermal sensitization study were evaluated and scored according to the following system:

No reaction	0
Very slight (barely perceptible) erythema, usually nonconfluent	0.5 (±)
Slight confluent or moderate patchy erythema	1
Moderate confluent erythema	2
Severe erythema, with or without edema, necrosis, or eschar formation .	3

When discussed in the text of this report, Grade 1 (slight confluent or moderate patchy) erythema will be referred to as slight erythema.

If edema, eschar formation, necrosis or other qualitative changes were observed, these findings were recorded.

5. Sensitization Rating

Redness at the challenge site clearly greater than that seen in irritation control animals would be considered an allergic response indicating elicitation of dermal sensitization in the guinea pigs.

L. Animal Disposition

Guinea pigs were killed by carbon dioxide asphyxiation and disposed of without necropsy following the termination of each range-finding study and following the sensitization study.

VIII. RESULTS AND DISCUSSION

A. Range-Finding Studies

Di-tert-Butyl Dicarbonate

The concentrations of the test material to be used during the induction and challenge phases of the study were determined from range-finding studies conducted with the material. The incidence of scores from range-finding studies with the test material can be found in TABLE 1. The individual dermal scores and any additional dermal findings recorded for the studies, and body weights recorded at the time of dosing can be found in TABLE 2.

The lowest concentration of the test material which was considered to produce minimal irritation was 15% (v/v) in 80% ethanol. This concentration was selected for use during the induction phase of the study. The highest concentration of the test material which was considered to produce no significant irritation (maximum nonirritant concentration) was 4.5% (v/v) in acetone. This concentration was selected for use during the challenge phase of the study.

DNCB

Based on the data from previous testing with DNCB, the lowest concentration of the positive control material which was considered to produce minimal irritation was 0.2% (w/v) in 80% ethanol. This concentration was selected for use during the

induction phase of the study. The highest concentration of the positive control material which was considered to produce no significant irritation (maximum nonirritant concentration) was 0.06% (w/v) in acetone. This concentration was selected for use during the challenge phase of the study.

B. Dermal Sensitization Study

1. Health and Body Weights

All guinea pigs survived through the induction and challenge phases of the sensitization study. No abnormal findings were noted during either the daily viability or the weekly general health examinations.

The body weight data recorded at the initiation and termination of the sensitization study can be found in TABLE 3.

All guinea pigs gained weight from initiation to termination of the study.

2. Induction Phase

Di-tert-Butyl Dicarbonate

The dermal scores and any additional dermal findings recorded during the induction phase for animals in Group 1 administered the test material can be found in TABLE 5.

Erythema was similar in the test animals in Group 1 and ranged from very slight (barely perceptible) to slight at 24 and 48 hours following the first induction exposure. The incidence of erythema observed during this interval indicated that an appropriate (minimally irritating) concentration of the test material had been selected for administration during the induction phase of the study.

An increase in the incidence and severity of erythema was noted by the second induction exposure. Severe erythema was observed at 24 and 48 hours following the second induction exposure. Additional dermal findings noted at test sites at this interval were edema, necrosis and eschar. Slight to severe erythema was observed in the animals at 24 hours and moderate to severe erythema was noted in the animals at 48 hours following the third exposure. Additional dermal findings noted at the test site following this exposure were edema, blanching and fissuring. The increased degree of response following the second and third exposures may have been indicative of cumulative irritation and/or sensitization resulting from administration of the test material. The dermal responses in some animals following the third induction exposure were less than responses following the second exposure because the application was made at a previously untreated (virgin) site at the time of the third exposure.

DNCB

The dermal scores and any additional dermal findings recorded during the induction phase for animals in Group 2 administered the positive control can be found in TABLE 8.

Erythema in the positive control animals (Group 2) ranged from very slight (barely perceptible) to slight at 24 and 48 hours following the first induction exposure. The incidence of erythema observed following this exposure indicated that an appropriate concentration of the positive control material had been selected for administration during the induction phase of the study.

Moderate to severe erythema was observed at 24 and 48 hours following the second induction exposure. Additional dermal findings noted at test sites at this interval were

edema, necrosis and eschar. Slight to moderate erythema was noted at 24 and 48 hours following the third exposure. Blanching and fissuring were observed in one animal following this exposure. The dermal responses in some animals following this third exposure were less than responses following the second induction exposure because the site of application was adjusted at the time of the third exposure.

The increase in the degree of dermal response by the second and third induction exposures was attributed to cumulative irritation at the sites and/or sensitization resulting from the administration of the DNCB.

3. Challenge Phase

Di-tert-Butyl Dicarbonate

The incidence of scores for Group 1 (test) and Group 3 (irritation control) animals which received the test material during the challenge phase can be found in TABLE 4. The individual dermal scores and any additional dermal findings recorded for animals in Group 1 can be found in TABLE 5. The individual dermal scores recorded for Group 3 animals (irritation controls) which received the test material can be found in TABLE 6.

Moderate erythema was observed in fifteen of twenty Group 1 animals (75%) at 24 hours following the challenge exposure. Severe erythema was observed in five of twenty animals (25%) at 24 hours. An additional dermal finding, edema, was noted in each of the animals at 24 hours following this exposure. Moderate erythema was observed in thirteen animals (65%) and severe erythema in seven animals (35%) at 48 hours. Additional dermal findings noted in animals at 48 hours were edema, blanching, necrosis and eschar.

Very slight erythema was observed in one of ten Group 3 irritation control animals (10%) at 24 and 48 hours following exposure to Di-tert-Butyl Dicarbonate during the challenge phase of the study. The low incidence of very slight (barely perceptible) erythema with no evidence of slight erythema observed in the Group 3 animals following the challenge exposure indicated that an appropriate (maximum nonirritating) concentration of the test material was selected for use during the challenge phase of the study.

The erythema observed in each of the Group 1 animals receiving Di-tert-Butyl Dicarbonate exceeded the degree of erythema noted in any irritation control animals. Since the dermal responses in the test (Group 1) animals clearly were increased when compared with the irritation control animals, the test material, Di-tert-Butyl Dicarbonate did elicit dermal sensitization in the test group animals.

DNCB

The incidence of scores for Group 2 (positive control) and Group 3 (irritation control) animals which received the positive control material, DNCB, during the challenge phase can be found in TABLE 7. The individual dermal scores and any additional dermal findings recorded for animals in Group 2 can be found in TABLE 8. The individual dermal scores recorded for Group 3 animals (irritation controls) which received the positive control material can be found in TABLE 9.

Slight to moderate erythema was observed in the ten Group 2 animals at 24 and 48 hours following the challenge exposure. Additional dermal finding, edema, was noted at test sites at 24 hours following exposure.

Very slight (barely perceptible) erythema was observed in two of ten Group 3 irritation control animals at 24 hours following exposure at challenge with DNCB. This very slight erythema persisted in these two animals through 48 hours. The incidence of very slight erythema with no evidence of slight erythema observed in the Group 3 irritation control animals following this exposure indicated that an appropriate (maximum nonirritating) concentration of the positive control material was selected for use during the challenge phase of the study.

The erythema observed in each of the ten Group 2 animals receiving DNCB exceeded the degree of erythema noted in any irritation control animals. Since the dermal responses in the positive control (Group 2) animals clearly were increased when compared with the irritation control animals, the DNCB did elicit dermal sensitization in the positive control group animals.

C. Sensitization Rating

Di-tert-Butyl Dicarbonate

The test material, Di-tert-Butyl Dicarbonate, did elicit dermal sensitization in the test animals. The dermal responses in the test (Group 1) animals clearly were increased when compared with the irritation control animals treated with the test material.

DNCB

The positive control material, DNCB, did elicit dermal sensitization in the positive control group animals. The dermal responses in the positive control (Group 2) animals clearly

were increased when compared with the irritation control animals treated with DNCB. This positive response demonstrated the susceptibility of the guinea pigs used in this study to dermal sensitization.

IX. CONCLUSION

The test material, Di-tert-Butyl Dicarbonate, demonstrated potential to produce dermal sensitization when administered by the modified Buehler method to Hartley guinea pigs.

TABLE 1

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

INCIDENCE OF DERMAL SCORES FOR ERYTHEMA

RANGE-FINDING STUDIES

Di-tert-Butyl Dicarbonate

Concentration	Interval	Dermal Scores 0	±	1	2	3	Number of Animals
100%	24 Hour			4			4
	48 Hour		2	2			
50%[a]	24 Hour			4			4
	48 Hour		1	3			
25%[a]	24 Hour			4			4
	48 Hour			4			
10%[a]	24 Hour		1	3			4
	48 Hour	1	1	2			
4.5%[a]	24 Hour	1	2	1			4
	48 Hour	2	2				
2%[a]	24 Hour	4					
	48 Hour	3	1				4
1%[a]	24 Hour	3	1				
	48 Hour	2	2				4
80% ethanol[b]	24 Hour	4					4
	48 Hour	4					

[a]Concentration (v/v) of Di-tert-Butyl Dicarbonate in 80% ethanol

[b]Served as a control

TABLE 1 (Continued)

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

INCIDENCE OF DERMAL SCORES FOR ERYTHEMA

RANGE-FINDING STUDIES

Di-tert-Butyl Dicarbonate

Concentration[a]	Interval	Dermal Scores					Number of Animals
		0	±	1	2	3	
10%	24 Hour	2	3	1			6
	48 Hour	2	4				
7%	24 Hour	2	2				4
	48 Hour	2	2				
4.5%	24 Hour	5	1				6
	48 Hour	4	2				
2%	24 Hour	6					6
	48 Hour	6					
1%	24 Hour	5	1				6
	48 Hour	4	2				

[a]Concentration (v/v) of Di-tert-Butyl Dicarbonate in acetone.

TABLE 2

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA (AND ANY ADDITIONAL DERMAL FINDINGS),
BODY WEIGHTS

RANGE-FINDING STUDIES

Di-tert-Butyl Dicarbonate

Range-Finding/May 23, 1990

Animal Number (Sex)	Body Weight (gram)	Concentration/Interval 100% 24 Hour	100% 48 Hour	50%[a] 24 Hour	50%[a] 48 Hour	25%[a] 24 Hour	25%[a] 48 Hour	Control 80% Ethanol 24 Hour	Control 80% Ethanol 48 Hour
26 (M)	295	1	1	1	1	1	1	0	0
64 (M)	272	1	1	1	±	1	1	0	0
80 (F)	250	1	±	1	1	1	1	0	0
100 (F)	258	1	±	1	1	1	1	0	0

Range-Finding/May 29, 1990

Animal Number (Sex)	Body Weight (gram)	Concentration/Interval 10%[a] 24 Hour	10%[a] 48 Hour	4.5%[a] 24 Hour	4.5%[a] 48 Hour	2%[a] 24 Hour	2%[a] 48 Hour	1%[a] 24 Hour	1%[a] 48 Hour
14 (M)	311	1	1	±	±	0	0	±	0
48 (M)	277	±	1	0	0	0	0	0	±
137 (F)	258	1	±	±	0	0	0	0	0
73 (F)	328	1	0	1	±	0	±	0	±

oncentration (v/v) of Di-tert-Butyl Dicarbonate in 80% ethanol

y: (M) = Male (F) = Female

TABLE 2 (Continued)

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA (AND ANY ADDITIONAL DERMAL FINDINGS), BODY WEIGHTS

RANGE-FINDING STUDIES

Di-tert-Butyl Dicarbonate

Range-Finding/June 13, 1990

Animal Number (Sex)	Body Weight (gram)	Concentration/Interval 10%[b] 24 Hour	10%[b] 48 Hour	4.5%[b] 24 Hour	4.5%[b] 48 Hour	2%[b] 24 Hour	2%[b] 48 Hour	1%[b] 24 Hour	1%[b] 48 Hour
47 (M)	477	1	±	0	0	0	0	±	0
52 (M)	411	0	0	0	0	0	0	0	0
29 (M)	545	±	±	±	0	0	0	0	0
101 (F)	352	±	0	0	0	0	0	0	±
134 (F)	421	±	±	0	±	0	0	0	0
98 (F)	372	0	±	0	±	0	0	0	±

Range-Finding/June 19, 1990

Animal Number (Sex)	Body Weight (gram)	Concentration/Interval 7%[b] 24 Hour	7%[b] 48 Hour
45 (M)	480	0	±
28 (M)	527	0	±
128 (F)	390	±	0
107 (F)	448	±	0

[b]Concentration (v/v) of Di-tert-Butyl Dicarbonate in acetone

Key: (M) = Male (F) = Female

TABLE 3

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

BODY WEIGHTS

	Individual Body Weight (gram)					
	MALES			FEMALES		
Group/Material	Animal Number	Prestudy	Terminal	Animal Number	Prestudy	Terminal
1 - Test/ Di-tert-Butyl Dicarbonate	116450	318	511	116460	314	457
	116451	322	579	116461	347	608
	116452	364	556	116462	350	551
	116453	300	496	116463	300	468
	116454	327	534	116464	313	452
	116455	340	634	116467	333	452
	116456	340	553	116466	301	412
	116457	346	521	116467	325	521
	116458	300	498	116468	300	468
	116459	332	517	116469	324	489
2 - Positive Control/ DNCB	116470	318	568	116475	331	493
	116471	348	564	116476	334	517
	116472	335	544	116477	375	581
	116473	305	588	116478	300	475
	116474	357	647	116479	302	468
3 - Irritation Control/ Di-tert-Butyl Dicarbonate and DNCB	116480	317	537	116485	331	535
	116481	334	538	116486	340	506
	116482	330	567	116487	316	472
	116483	328	602	116488	330	543
	116484	311	565	116489	321	489

TABLE 4

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

INCIDENCE OF DERMAL SCORES FOR ERYTHEMA AT CHALLENGE

Di-tert-Butyl Dicarbonate

Group/Material	Interval	Dermal Scores					Number of Animals
		0	±	1	2	3	
1 - Test/ Di-tert-Butyl Dicarbonate (4.5%[a])	24 Hour				15	5	20
	48 Hour				13	7	20
3 - Irritation Control/ Di-tert-Butyl Dicarbonate (4.5%[a])	24 Hour	9	1				10
	48 Hour	9	1				10

[a]Concentration (v/v) of Di-tert-Butyl Dicarbonate in acetone

TABLE 5

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA (AND ANY ADDITIONAL DERMAL FINDINGS)

INDUCTION AND CHALLENGE PHASES

Di-tert-Butyl Dicarbonate (GROUP 1)

Animal Number (Sex)	Induction (15%[a]) 1		2		3[c]		Challenge (4.5%[b])	
	24 Hour	48 Hour	24 Hour	48 Hour	24 Hour	48 Hour	24 Hour	48 Hour
116450 (M)	0	0	3ED,NE,ES	3ED,NE,ES	2	2	2ED	2
116451 (M)	±	±	3ED,NE,ES	3ED,NE,ES	1	2FI	2ED	2
116452 (M)	±	1	3ED,NE,ES	3ED,NE,ES	2	2	2ED	2ED
116453 (M)	±	±	3ED,NE,ES	3ED,NE,ES	2	3FI,ED	2ED	2
116454 (M)	±	1	3ED,NE,ES	3ED,NE,ES	2	2	2ED	2
116455 (M)	±	±	3ED,NE,ES	3ED,NE,ES	2	2	3ED	3ED
116456 (M)	±	±	3ED,NE,ES	3ED,NE,ES	2	2	2ED	2
116457 (M)	±	1	3ED,NE,ES	3ED,NE,ES	2	2	2ED	2
116458 (M)	±	1	3ED,NE,ES	3ED,NE,ES	2ED	2ED,FI	2ED	2ED
116459 (M)	1	1	3ED,NE,ES	3ED,NE,ES	2ED	2ED,FI	3ED	3ED
116460 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2ED	2ED,BL	2ED	3ED,NE,ES
116461 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2ED	2	2ED	2
116462 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2	2ED,FI	2ED	2
116463 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2ED	3BL,ED,FI	2ED	3ED,BL
116464 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2ED	3FI,ED	2ED	2ED
116465 (F)	±	1	3ED,NE,ES	3ED,NE,ES	2ED	2FI,ED	3ED	3ED
116466 (F)	0	±	3ED,NE,ES	3ED,NE,ES	2ED	2FI,ED	3ED	3ED
116467 (F)	±	±	3ED,NE,ES	3ED,NE,ES	3ED	3FI,ED	2ED	2
116468 (F)	1	1	3ED,NE,ES	3ED,NE,ES	3ED	3FI,ED	3ED	3ED
116469 (F)	±	±	3ED,NE,ES	3ED,NE,ES	2ED	2FI,ED	2ED	2ED

[a]Concentration (v/v) of Di-tert-Butyl Dicarbonate in 80% ethanol

[b]Concentration (v/v) of Di-tert-Butyl Dicarbonate in acetone

[c]The site of application for each animal was adjusted during the third induction period to avoid reapplication of the material to severely irritated or damaged skin.

Key: (M) = Male (F) = Female
(ED) = Edema (FI) = Fissuring (BL) = Blanching (NE) = Necrosis (ES) = Eschar

TABLE 6

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA

IRRITATION CONTROLS (CHALLENGE PHASE)

Di-tert-Butyl Dicarbonate (GROUP 3)

Animal Number (Sex)	Challenge (4.5%[a]) 24 Hour	48 Hour
116480 (M)	0	0
116481 (M)	0	0
116482 (M)	±	±
116483 (M)	0	0
116484 (M)	0	0
116485 (F)	0	0
116486 (F)	0	0
116487 (F)	0	0
116488 (F)	0	0
116489 (F)	0	0

[a]Concentration (v/v) of Di-tert-Butyl Dicarbonate in acetone

Key: (M) = Male (F) = Female

TABLE 7

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

INCIDENCE OF DERMAL SCORES FOR ERYTHEMA AT CHALLENGE

DNCB

Group	Material	Interval	Dermal Scores 0	±	1	2	3	Number of Animals
2 - Positive Control	DNCB (0.06%[a])	24 Hour			6	4		10
		48 Hour			5	5		10
3 - Irritation Control	DNCB (0.06%[a])	24 Hour	8	2				10
		48 Hour	8	2				10

[a]Concentration (w/v) of DNCB in acetone

TABLE 8

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA (AND ANY ADDITIONAL DERMAL FINDINGS)

INDUCTION AND CHALLENGE PHASES

DNCB (GROUP 2)

Animal Number (Sex)	Induction (0.2%[a]) 1		2		3[c]		Challenge (0.06%[b])	
	24 Hour	48 Hour	24 Hour	48 Hour	24 Hour	48 Hour	24 Hour	48 Hour
116470 (M)	±	±	2ED	3ED,NE	2	2	2ED	2
116471 (M)	1	1	3ED,NE	3ED,NE,ES	1	1	2ED	2
116472 (M)	±	±	2ED	2ED	1	2BL,FI	1	1
116473 (M)	±	±	3ED,NE,ES	3ED,NE,ES	2	2	1	1
116474 (M)	±	1	3ED	3ED,NE	1	1	1	1
116475 (F)	±	0	2ED	2ED	1	1	1	1
116476 (F)	±	±	3ED	3ED,NE	1	1	2ED	2
116477 (F)	1	±	3ED,NE	3ED,NE	2	2	1	1
116478 (F)	1	1	3ED,NE,ES	3ED,NE,ES	1	1	1	2
116479 (F)	±	1	3ED,NE	3ED,NE	1	1	2ED	2

[a]Concentration (w/v) of DNCB in 80% ethanol
[b]Concentration (w/v) of DNCB in acetone
[c]The site of application for each animal was adjusted during the third induction period to avoid reapplication of the material to severely irritated or damaged skin.

Key: (M) = Male (F) = Female
(ED) = Edema (NE) = Necrosis
(ES) = Eschar (BL) = Blanching
(FI) = Fissuring

TABLE 9

DERMAL SENSITIZATION STUDY
(CLOSED-PATCH REPEATED INSULT)
IN GUINEA PIGS WITH DI-TERT-BUTYL DICARBONATE

DERMAL SCORES FOR ERYTHEMA

IRRITATION CONTROLS (CHALLENGE PHASE)

DNCB (GROUP 3)

Animal Number (Sex)	Challenge (0.06%[a]) 24 Hour	48 Hour
116480 (M)	0	0
116481 (M)	0	0
116482 (M)	±	±
116483 (M)	0	0
116484 (M)	0	0
116485 (F)	0	0
116486 (F)	0	0
116487 (F)	±	±
116488 (F)	0	0
116489 (F)	0	0

[a]Concentration (w/v) of DNCB in acetone

Key: (M) = Male (F) = Female

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
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NOV 17 1994

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Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

13092 A

Triage of 8(e) Submissions

Date sent to triage: OCT 14 1994

(NON-CAP) CAP

Submission number: 13092 A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

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Notes:

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CECATS DATA:
Submission # 8EHQ- 0694 - 13092 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: First Chemical Corporation

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB DATE: 06/29/94 OTS DATE: 06/29/94 CSRAD DATE: 07/21/94

CHEMICAL NAME: CAS#

24424-99-5

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	(0243)	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	(0248)	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	(0251)	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	(0228)	ALLERG (ANIMAL)	(01 02 04)			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	(YES)	YES (DROP/REFER)	GP	LOW	Intermediate for peptides	
	NO	NO (CONTINUE)		MED		
	DETERMINE	REFER:		HIGH		

COMMENTS: Non-CAP

8(e) 8(E)-13092A	TRIAGE ASSESSMENT
TOX CONCERN H	

SKIN SENSITIZATION IN GUINEA PIGS IS HIGH CONCERN. 5/20 ANIMALS SHOWED SEVERE ERYTHEMA AND 15/20 SHOWED MODERATE ERYTHEMA AT 24 HOURS AFTER CHALLENGE. ADDTITIONAL DERMAL FINDINGS AT 48 HOURS WERE EDEMA, BLANCHING, NECROSIS AND ESCHAR. DERMAL SIGNS OF MODERATE TO SEVERE ERYTHEMA, EDEMA, BLANCHING AND FISSURING WERE NOTED DURING THE INDUCTION PHASE WITH INCREASING DEGREE OF RESPONSE AFTER EACH APPLICATION.